

U.S. Food & Drug Administration
Center for Food Safety & Applied Nutrition
Office of Food Additive Safety
July 2001

Guidance for Industry⁽¹⁾
Providing Regulatory Submissions to
Office of Food Additive Safety in
Electronic Format -- General Considerations

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Draft released for comment July 2001

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the Federal Register of the notice announcing the availability of the draft guidance. Submit Comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD, 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the Federal Register.

For questions on the content of the draft document contact the Electronic Submissions Coordinator, Office of Food Additive Safety, Center for Food Safety and Applied Nutrition, E-Mail: elecsub@cfsan.fda.gov.

Additional contact information.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
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GDL-1

DRAFT GUIDANCE

This draft guidance represents FDA's current thinking on regulatory submissions in electronic format. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirement of applicable statutes and regulations. The draft guidance is being distributed for comment purposes in accordance with FDA's Good Guidance Practices (65 FR 56468; September 19, 2000).

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I. INTRODUCTION

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This is one in a series of guidance documents that the Office of Food Additive Safety (OFAS) will provide to assist you when making regulatory submissions in electronic format to OFAS, Center for Food Safety and Applied Nutrition (CFSAN), Food and Drug Administration (FDA). In some cases,

the guidance for one center differs from that for another center because of differences in procedures and in the computer infrastructures in the centers. OFAS will work to minimize these differences wherever possible.

OFAS intends to update regularly its guidance documents on electronic regulatory submissions to reflect the evolving nature of the technology involved and the experience of those using this technology.

II. BACKGROUND

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In the *Federal Register* of March 20, 1997 (62 FR 13430), the FDA published the Electronic Records; Electronic Signatures final rule (21 CFR Part 11). This final rule provided for the voluntary submission of parts or all of regulatory records in electronic format without an accompanying paper copy. Publication of this regulation resulted in a series of related actions by the Agency:

March 1997:

The Agency established public docket number 92S-0251 to provide a permanent location for a list of the Agency units that are prepared to receive electronic submissions and the specific types of regulatory records that can be accepted in electronic format (62 FR 13467, March 20, 1997). This docket can be accessed on the Internet at <http://www.fda.gov/ohrms/dockets/dockets/92s0251/92s0251.htm>.

September 1997:

CDER published guidance for industry entitled "Archiving Submissions in Electronic Format - NDAs"⁽²⁾ (62 FR 49695, September 23, 1997) to assist applicants wanting to make electronic submissions of case report forms (CRFs) and case report tabulations (CRTs) as part of the NDA archival submission.

April 1998:

CDER issued draft guidance for industry, *Providing Regulatory Submission in Electronic Format - NDAs*, which expanded the September 1997 guidance by providing information of submitting a **complete** archival copy of the NDA in electronic format (63 FR 17185; April 8, 1998)

June 1998:

CDER published the following draft guidances to assist applicants in their efforts to submit electronic documents to the Center for review and archive as part of their Biologics License Application (BLA) or Product License Application (PLA)/Establishment License Application (ELA) submissions:

Electronic Submissions of a BLA, PLA / ELA to the Center for Biologics Evaluation and Research (63 FR 29741; 6/1/98).

Electronic Submissions of Case Report Forms (CRFs), Case Report Tabulations (CRTs) and Data to the Center for Biologics Evaluation and Research (63 FR 29739; 6/1/98).

Pilot Program for Electronic Investigational New Drug (eIND) Applications for Biological Products (63 FR 29740; 6/1/98).

Instructions for Submitting Electronic Lot Release Protocols to the Center for Biologics Evaluation and Research (63 FR 29742; 6/1/98).

January 1999:

CDER and CBER finalized a joint guidance on general considerations for **electronic submissions**. (64 FR 4433; 1/28/99) Subsequent guidance will focus on specific submission types.

July 1999:

The agency published a guidance entitled *Electronic Policy: Electronic Records; Electronic Signatures-Compliance Policy Guide; Guidance for FDA Personnel* (62 FR 39146; July 21, 1999).

In addition to the present draft guidance and the draft guidance regarding food additive and color additive petitions, OFAS plans to publish guidance documents on electronic submissions to provide guidance on the following:

- Generally Recognized as Safe Notices, GRNs
- Biotechnology Notifications, BNFs
- Food Contact Notifications, FCNs

As individual documents are completed, we anticipate that they will be issued first in draft for comment, then finalized and added to the series. The guidance will be updated regularly to reflect the continuously evolving nature of the technology and experience of those using this technology.

III. HOW DO ELECTRONIC SUBMISSIONS RELATE TO 21 CFR PART 11?

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FDA's part 11 regulations (21 CFR part 11), among other things, set forth the criteria under which records, required to be submitted to FDA, may be submitted in electronic format in lieu of paper. Section 11.2(b) states that, "for records submitted to the agency, persons may use electronic records in lieu of paper records..., in whole or part, provided that: (1) the requirements of part 11 are met; and (2) The documents or parts of documents to be submitted have been identified in public docket No. 92S-0251 as being the type of submission the agency accepts in electronic form."

IV. WHAT FILE FORMATS SHOULD I USE FOR ELECTRONIC DOCUMENTS?

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Regulations in 21 CFR Part 11 require that the Agency be able to generate from any document provided in electronic format an accurate and complete paper copy that is both legible ("human

readable") and suitable for inspection, review, and copying. Therefore, documents submitted in electronic format should:

- Enable the user to easily view a clear and legible copy of the information.
- Enable the user to print each document page by page, as it would have been provided in paper, maintaining fonts, special orientations, table formats, and page numbers.
- Include a well-structured table of contents and allow the user to navigate easily through the submission.
- Allow the user to copy text and images electronically into common word processing documents.

To achieve the above goals, all documents will be submitted electronically in Portable Document Format (PDF). OFAS is prepared to archive documents provided as PDF files. PDF is an open, published format created by Adobe Systems Incorporated (<http://www.adobe.com>). It is not necessary to use a product from Adobe or from any specific company to produce the PDF documents. PDF has been accepted as the standard for providing documents in electronic format by the International Conference on Harmonisation (ICH).

The following recommendations will help create PDF files that can be reviewed and archived.

A. Version

All PDF files using version 4.0 or 5.0 of the Acrobat Reader will be acceptable with the search plug in. You should not submit any PDF files requiring additional software to read and navigate them.

B. Fonts

PDF viewing software automatically substitutes a font to display text if the font used to create the text is unavailable on the reviewer's computer. Font substitution can affect a document's appearance and structure, and in some cases it can affect the information conveyed by a document. There is no guarantee of the availability of any one font. Therefore, all fonts should be embedded when the files are created to ensure that those fonts will always be available to the reviewer. When embedding fonts, all characters for the font should be embedded, not just a subset of the fonts being used in the document.

Unfortunately, font embedding does not solve the problems that occur when a reviewer tries to paste text from a PDF document into another software format. If the font is not available on the reviewer's computer, font substitution results even if the fonts are embedded. For this reason, please restrict the fonts used in documents to one of the following fonts listed in Table 1. OFAS still asks that you prepare and embed the fonts so they are available for printing older archival files.

Table 1: List of Acceptable Fonts

Font Type	Font Name
San Serif	AdobeSansMM -- (Adobe Sans Multiple Master)
	Arial BolitaMT -- (Arial Bold Italic (From Monotype))
	Arial BolMT -- (Arial Bold Monotype)
	ArialtaMT -- (Arial Italic (Monotype))
	ArialMT -- (Arial (Monotype))

Non Proportional	Couri -- (Courier)
	CouriBol -- (Courier Bold)
	CouriBolObl -- (Courier Bold Oblique)
Serif	AdobeSerifMM - (Adobe Serif Multiple Masters)
	Times NewRomPSBolitaMT - (Times New Roman Bold Italic)
	TimesNewRomPSBolMT - (Times New Roman Bold)
	TimesNewRomPSItaMT - (Times New Roman Italic)
	TimesNewRomPSMT - (Times New Roman)
	TimesNewRoman
Other	Symbo (Symbol)
	ZapfDin (Zapf Dingbats)

Resizing a document because the contents are too small to read is inefficient. The font, Times New Roman, 12-point font, the font used for this document, is adequate in size for reading narrative text. Although sometimes tempting for use in tables and charts, fonts smaller than 12 point should be avoided whenever possible. When choosing a point size for tables, a balance should be made between providing sufficient information on a single page that may facilitate data comparisons while still achieving a point size that remains legible. The corollary of this is that in making point size larger, more tables may be necessary which may complicate data comparisons since data may now be included in separate tables on separate pages. Generally, point sizes 9-10 are acceptable in tables, but smaller point sizes should be avoided.

We recommend the use of a black font color. Blue font may be used for hypertext links (preferred for submissions to OFAS). If a font color other than black is used, avoid light colors that do not print well on grayscale printers. You should test the color reproduction prior to submission by printing sample pages from the document using a grayscale printer.

C. Page Orientation

Pages should be properly oriented. For example, set the page orientation of landscape pages to landscape prior to saving the PDF document in final form to ensure correct page presentation.

D. Page Size and Margins

The print area for pages should fit on a sheet of paper that is 8.5 inches by 11 inches. Allow a margin of at least 1 inch on left side of page and 3/8 of an inch on all other sides to avoid obscuring information if the pages are subsequently printed and bound. For pages in landscape orientation, allow 3/4 of an inch at the top to allow more information to be displayed legibly on the page. It is acceptable that header and footer information appear within these margins as long as they are not lost upon printing.

E. Source of Electronic Document

PDF documents produced by scanning paper documents are usually inferior to those produced from an electronic source document. Scanned documents are more difficult to read and should be avoided if

at all possible. If optical character recognition (OCR) software is used, verify that all imaged text converted by the software is accurate.

F. Methods for Creating PDF Documents and Images

Choose a method for creating PDF documents that produces the best replication of a paper document. Ensure that the paper and PDF versions of the document are the same by printing the document from the PDF version.

Documents that are available only in paper should be scanned at resolutions that will ensure the pages are legible both on the computer screen and when printed. At the same time, limit the file size. OFAS recommends scanning at a resolution of 300 dots per inch (dpi) to balance legibility and file size. The use of grayscale or color is discouraged because of file size. However, if grayscale or color is necessary, the following paragraphs provide preliminary recommendations and specific guidance documents provide additional details. After scanning, avoid resampling to a lower resolution.

The optimal image resolution and bit depth depend in large part on the actual need for viewing the image. You should not provide images at high resolution and depth without determining the need. High resolution and depth images result in large files, taking up valuable storage space. It is better to provide samples of the images at various resolutions and depths prior to sending in the actual submissions to determine the optimal image resolution and depth to meet the review need.

When creating PDF files containing images, do not resample images. Resampling does not preserve all of the pixels in the original. For PDF images, use one of the following lossless compression techniques (with the exception that, when submitting to OFAS, standard radiographic images, PET, and SPECT images should not be compressed).

- For lossless compression of color and grayscale images, use ZLIB/DEFLATE. This alternative is specified in Internet RFC 1950 and RFC 1951 (<http://info.internet.isi.edu/in-notes/rfc/files/rfc1950.txt>).
- For lossless compression of black and white images, use the CCITT Group 4 Fax compression technique. It is specified as CCITT recommendations T.6 (1988) - *Facsimile coding schemes and coding control functions for Group 4 facsimile apparatus*.

Paper documents containing handwritten notes should be scanned at 300 dpi. Handwritten notes should be done in black ink for clarity.

For photographs, the image should be obtained with a resolution of 600 dpi. If black and white photos are submitted, consider 8-bit gray scale images. If color photos are submitted, consider 24-bit RGB images. A captured image should not be subjected to non-uniform scaling (i.e., sizing). Gels and karyotypes should be scanned directly, rather than from photographs.

Plotter output graphics should be scanned or captured digitally at 300 dpi.

High-pressure liquid chromatography or similar images should be scanned at 300 dpi.

When color is important in the review of a file, make sure that the colors are an accurate representation of the actual image. Since color varies from monitor to monitor, it is difficult to assure

the reviewer will see exactly the same color as in the actual image. However, for printing, there is more control over the color if the CMYK color model is used as opposed to the RGB model. Since PDF uses the color profile provided by CMYK, use the Pantone Matching and this will assure color consistency for printing. PDF also uses the ICC color profile specifications when PDF documents are printed.

G. Hypertext Linking and Bookmarks

Hypertext links and bookmarks are techniques used to improve navigation through PDF documents. Hypertext links can be designated by rectangles using thin lines or by blue text (the latter is preferred by OFAS). In OFAS, use invisible rectangles for hypertext links in a table of contents to avoid obscuring text. Recommendations for hypertext linking and bookmarks are provided in the guidance for the specific submission type.

In general, for documents with a table of contents, provide bookmarks and hypertext links for each item listed in the table of contents including all tables, figures, publications, other references, and appendices. These bookmarks and hypertext links are essential for the efficient navigation through documents. In general, including a bookmark to the main table of contents for a submission or item is helpful. Make the bookmark hierarchy identical to the table of contents.

Avoid using bookmark levels in addition to those present in the table of contents.

Each additional level increases the need for space to read the bookmarks. Using no more than 4 levels in the hierarchy is recommended.

Hypertext links throughout the body of the document to supporting annotations, related sections, references, appendices, tables, or figures that are not located on the same page are helpful and improve navigation efficiency. Use relative paths when creating hypertext linking to minimize the loss of hyperlink functionality when folders are moved between disk drives. Absolute links that reference specific drives and root directories will no longer work once the submission is loaded onto our network servers.

When creating bookmarks and hyperlinks, choose the magnification setting *Inherit Zoom* so that the destination page displays at the same magnification level that the reviewer is using for the rest of the document.

H. Page Numbering

It is easier to navigate through an electronic document if the page numbers for the document and the PDF file are the same. To accomplish this, the initial page of the paper document should be numbered page with Bates numbering format, e.g., 000001.

There are two circumstances where this may not be true.

1. When a document is split because of its size (e.g., greater than 50 MB), the second or subsequent file should be numbered consecutively to that of the first or preceding file.
2. When several small documents with their own internal page numbering have been brought together into a single file, it is not necessary to provide additional page numbering for each

document, although the start of each sub document should be bookmarked. For example, if an original protocol is added as an appendix to a study report, you should not add page numbers to the original protocol so the page numbers are consecutive to the rest of the study report. Provide a bookmark to the original protocol.

I. Document Information Fields

Document information fields are used to search for individual documents and to identify the document when found. Recommendations for the document information fields will be provided in the guidance for the specific-submission type.

J. Open Dialog Box

The open dialog box sets the document view when the file is opened. The initial view of the PDF files will be set as *Bookmarks* and *Page*. If there are no bookmarks, set the initial view as *Page* only. Set the *Magnification* and *Page Layout* to default.

K. Naming PDF Files

Recommended names for folders and selected files in individual guidances for specific submission types have been included. For uniformity, use the specific naming conventions when they are provided. Reviewers are trained to look for these folders and files, and using the recommended names will help to avoid misunderstandings, improve communication, and speed the review of a submission.

The files and folders name can contain up to 80 characters, including spaces, however, it cannot contain any of the following characters: \ / : * ? < > | " % # +.

L. Security

Do not include any security settings or password protection for PDF files. Allow printing and selecting text and graphics. The OFAS internal security and archival processes will maintain the integrity of the submitted files. A read-only copy of the files, generated from the submitted files, will be provided to the reviewer.

M. Plug Ins

It is acceptable to use plug-ins to assist in the creation of a submission. However, the review of the submission should not require the use of any plug ins, in addition to those provided with Acrobat Reader 4 or 5 because we are not prepared to archive additional plug-in functionality.

N. Electronic Signatures

We are developing procedures for archiving documents with electronic signatures. Until those procedures are in place, documents for which regulations require a signature, such as certifications, should be accompanied by a paper copy that includes the handwritten signature and the submission identifier (e.g., petition name).

V. WHAT FILE FORMATS SHOULD I USE FOR ELECTRONIC DATASETS?

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Regulations in 21 CFR Part 11 require all datasets provided in electronic format to provide an accurate and complete copy of the data suitable for inspection, review, and copying. Currently, we are able to accept and archive datasets in SAS System XPORT transport format (Version 5 SAS transport file). OFAS plans on providing guidance for additional file format types for datasets (see Section B, below).

A. SAS System XPORT Transport Format (Version 5 SAS Transport Format)

SAS XPORT transport format, also called Version 5 SAS transport format, is an open format published by the SAS Institute. The description of this SAS transport file format is in the public domain. Data can be translated to and from this SAS transport format to other commonly used formats without the use of programs from SAS Institute or any specific vendor.

You should follow the recommendations in this section to create SAS transport files that we can review and archive.

1. Version

In SAS, SAS XPORT transport files are created by PROC XCOPY in Version 5 of SAS software and by the XPORT engine in Version 6 and higher of SAS Software. We are unable to archive SAS Transport files processed by the CPORT engine.

You can find the record layout for SAS XPORT transport files in SAS technical support TS-140. This document and additional information about the SAS Transport file layout can be found on the SAS world wide web page at <http://www.sas.com/fda-esub>.

2. Transformation of Datasets

We use a variety of software tools to analyze the datasets. Stat/Transfer from Circle Systems and DBMS/copy from Conceptual Software Inc., are two programs used to transfer data to various formats used for analysis. SAS Viewer version 7 is used to open SAS transport files directly.

3. Naming SAS Transport Files

All SAS transport files should use *xpt* as the file extension.

4. Compression of SAS Transport Files

The SAS transport files should not be compressed. There should be one transport file per dataset.

5. Content Of Datasets and Organization

You should provide a single transport file for each dataset. Many of the software tools used by the reviewers require datasets to be loaded into random access memory (RAM) prior to opening

the file. Therefore, dataset files should be organized so that their size is generally less than 50 MB per file. Datasets divided to meet the maximum size restrictions should contain the same variable presentation so they can be easily merged, joined and concatenated.

OFAS recommends that you discuss the content of the datasets with the review division prior to submission.

B. Other Dataset Formats

At times, we will identify additional file formats that you may consider using to address specific functions not previously described. For example, we use an ASCII file format called Molfile to digitally represent two and three dimensional chemical structures. OFAS uses the base structure, not including identification of the salt or chimeric codes, to identify product ingredients. This identification is used to improve the linking of information found in other databases.

The file format called Molfile is in the public domain and was developed by Molecular Design Limited, (MDL) in the late 70s. Currently, the company, now named Molecular Design Limited Information Systems, is a wholly owned subsidiary of Elsevier Science. Technical information about the Molfile format can be found at the MDL web site at <http://www.mdli.com/downloads/literature/ctfile.pdf>.

Molfiles are generated by chemical structure drawing programs. The most common drawing programs ISIS/Draw from MDL and ChemDraw Pro from Cambridge Soft (<http://www.cambridgesoft.com>) create Molfiles. A free copy of ISIS/DRAW for your personal use may be obtained from MDL web site at <http://www.mdli.com/downloads/isisdraw.html>.

Molfiles can be viewed and reformatted using Chime, a free plug in to Microsoft's Internet Explorer and Netscape Communicator from MDL. You can download the plug in at <http://www.mdli.com/downloads/chime.html>.

Molfiles can be searched using database programs such as ISIS Base. Additional information about this database program can be found at the MDL web site at <http://www.mdli.com>.

Data may also be submitted in spreadsheets, such as Excel, or in table format in *pdf* form.

VI. WHAT ARE THE PROCEDURES FOR SENDING ELECTRONIC SUBMISSIONS FOR ARCHIVE?

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Electronic submissions should be provided on physical media, such as floppy disk, CD-ROM, or digital tape. You should refer the guidance of the specific submission type for the appropriate procedures. Currently, OFAS only accepts a submission provided in physical media. All submissions should be sent directly to the Office of Food Additive Safety. The procedure for handling paper submissions is unchanged from the past.

You must send an electronic submission or a paper submission to:

Office of Food Additive Safety

200 C St. SW, HFS-200
Washington, DC 20204

You should communicate with OFAS prior to submitting an electronic document, notifying us of your intention to submit an electronic document in advance of the target date for the submission.

OFAS will schedule a teleconference or meeting between petitioners and the appropriate OFAS staff. The objective of the teleconference is to convey information relating to the proposed electronic submission's management paradigm, content, format, and structure. Moreover, OFAS will discuss any issues specific to your submission that may not have been fully addressed in this general considerations guidance. The amount of time that will be needed to ensure that the document is ready for submission will depend on the complexity of the document and experience of the petitioner in preparing petitions/notification.

VII. WHAT TYPE OF MEDIA SHOULD I USE?

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There are 3 methods for sending submissions electronically. They are Electronic Data Interchange (EDI), Physical Media, or E-mail. Currently, OFAS is only accepting a submission provided on physical media and it intends to develop other methods for acceptance at a later date.

OFAS is prepared to accept electronic submissions provided on the physical media listed in the table below. To optimize processing efficiency, OFAS recommend choosing physical media with a capacity most appropriate to the size of the submission. Whenever possible, applicants should choose media capable of holding the submission on the *fewest* number of units.

Recommendations for Media

Size of Submission	Media and Format	Units
Less than 10MB	3.5 inch DOS Formatted Floppy Disks	1 to 10
Less than 3.25GB	CD-ROM ISO 9660	1 to 5 CDs
Greater than 3.25GB	Digital Tape - Digital Equipment Corp. OPENVMS with VMS backup or NT server 4.0 with NT backup or backup exec.	No limit

VIII. HOW SHOULD I PREPARE THE MEDIA FOR ELECTRONIC SUBMISSIONS FOR ARCHIVE?

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You should send all electronic media adequately secured in a standard binder marked clearly on the outside ELECTRONIC REGULATORY SUBMISSION FOR ARCHIVE. CDs should be packaged carefully to ensure that they arrive in a usable condition. Particularly vulnerable are diskettes and CD jewel cases shipped in envelopes without bubble-type protective material or stiff backing. The use of a jiffy-type bag by itself to ship media will not provide adequate protection for shipping electronic media.

The first binder with electronic media should include only a paper copy of the cover letter for the submission and the electronic media for archiving. Please attach labels to the media including the CD jewel cases. Label the media with the following:

- Submission identifier (e.g., Petition, Notification number)
- Chemical /Ingredient Name
- Company Name
- Submission date: in the format of DD-MMM-YYYY (for example, 01-Jan-2000).
- Disk/CD-ROM/tape number (the number should include the total number submitted such as Disk # of #).

When sending CD-ROMs to OFAS, number them from 0.001 through 0.XXX for the original submission, and 1.001 through 1.XXX for subsequent submissions with additional information.

IX. HOW DOES OFAS PROCESS ELECTRONIC SUBMISSIONS FOR ARCHIVE?

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When an electronic submission arrives in OFAS, it is copied both to archives and to a network server to create a read-only copy for the reviewer

The structure and content of electronic submissions to OFAS should be based upon the application (e.g., Petition, Notification, etc.). Subsequent to the delivery of the electronic application, any additional electronic and/or paper information will be added both to archived copy and to the existing network copy of the submission and made available to appropriate managers and reviewers. The root directory of an electronic application should contain a roadmap.pdf file to orient the review team to the original application and to any and all subsequent information added to the application.

OFAS suggests that a roadmap.pdf file be used to establish hypertext links to the application's main table of contents, and to the applications folders and files. This roadmap or home page should be updated and resubmitted as additional information is added to the application.

The roadmap file should not contribute in any way to the content of what is under review. It is a map, intended to facilitate navigation through the contents of an application. The application's roadmap.pdf file should be easily updated or modified, for example, using the Replace File command under the Document menu option in Adobe Exchange. This function will automatically replace the old hypertext links to previously submitted sections of the application, leaving only the task of creating the new links corresponding to newly submitted information.

In addition to providing a navigable guide to the application, the roadmap.pdf file should include the sponsor's submission date in the DD-MMM-YYYY format. (e.g., 01-Jan-2000). The contents of the original application and any subsequent amendments to that application should be briefly described in a roadmap.pdf table. The location of these files and folders on the submitted media should be indicated in the roadmap.pdf. Where portions of an application have been submitted only as a paper documents, they should be included in the roadmap and table of contents and tagged as paper only.

X. WHAT IF I HAVE A QUESTION?

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You may direct questions regarding the preparation of submissions in electronic format in CFSAN to the Electronic Submissions Coordinator email elecsub@cfsan.fda.gov.

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1. This guidance was prepared by the Office of Food Additive Safety (OFAS), Center for Food Safety and Applied Nutrition (CFSAN) at the Food and Drug Administration (FDA). This guidance document represents the Agency's current thinking on regulatory submissions in electronic format. The current document is being published by the OFAS. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute and regulations.

On June 1, 1998, the President instructed all Federal agencies to ensure the use of plain language in all new documents. This guidance reflects Agency efforts to comply with the President's plain language initiative 5.

2. New Drug Applications

*Office of Food Additive Safety
HFS-200
200 C Street, SW
Washington, DC 20004
(Tel) 202-418-3100
(Internet) <http://www.cfsan.fda.gov/~dms/opa-toc.html>*

Food Additives and Premarket Approval

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